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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,319	11/02/2000	Hiroo Kumagai	1514-00	4918

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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/704,319	Applicant(s) KUMAGAI ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,12 and 13* is/are rejected.

7)☒ Claim(s) *1,3,4,6,12 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Amendment B, filed 4/15/03, has been entered into the record.

B. The Declaration of Mr. Kenji Takamori, filed 4/15/03, has been entered into the record.

C. Claims 1-4 and 6 were pending in the application. In Amendment B, Applicants cancelled claim 2 and added new claims 12 and 13. Therefore, claims 1, 3, 4, 6, 12 and 13 are pending and are the subject of this Office Action.

D. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

E. Though not forming the basis for a rejection or objection, the syntax of claim 6 would be improved by replacing the phrase "or pregnancy" with "and pregnancy" since all of the claimed diseases are part of a group. The use of "and" instead of "or" would maintain the consistency in the claim, as well as with claim 12.

F. Though not forming the basis of a rejection or objection, the syntax of claims 6 and 12 could be improved by amending the claim to place a colon after the phrase "consisting of" which would indicate a list of items (e.g. diseases) follows. This would also maintain parallel sentence structure with claims 1 and 13 which use a colon after "comprising the steps of" to indicate a list of steps follows.

2. Claim Objections

A. The objection to claim 6 has been withdrawn in view of Applicants' amendment to the term "scbies" to recite "scabies."

B. Claim 1 and 13 are objected to since the syntax could be improved by removing the word "and" after the word "tissue" since the word "and" should only be used to separate the last two method steps in a claim. Furthermore, the syntax of the claims could be improved by labeling each of the method steps as individual parts, for example:

"(a) measuring concentrations...

(b) calculating the ratio..."

If Applicants do not wish to label the individual steps in claim 1, the phrase beginning with "calculating" should be indented to be consistent with the other method steps in the claim. Claims 3, 4, 6 and 12 are also objected to since they depend from claim 1.

C. Claim 3, 4, 6 and 12 are objected to since the syntax could be improved by replacing the phrase "a method according to" with "the method according to."

D. Claims 1, 3, 4, 6, 12 and 13 are objected to since the syntax could be improved by amending the phrase in claim 1 and 13 to recite the singular "peptide" instead of the plural "peptides." For example, "measuring concentrations of at least one κ-opioid peptide[s] and at least one [of] δ-opioid peptide[s], μ-opioid peptide[s], [and] or nociceptin." Following this suggestion would also clarify claims 3 and 4 since claim 3 recites, and claim 4 implies (e.g. dynorphin A in claim 4), both the singular "peptide" and the plural "peptides." For example, claim 4 should be amended from "wherein said μ-opioid peptides to be measured are β-endorphin and said κ-opioid peptides are dynorphin A" to "wherein said μ-opioid peptide[s] to be measured [are] is β-endorphin and said κ-opioid peptide[s] [are] is dynorphin A." Claims 6 and 12 are also objected to since they depend from claim 1.

E. Claim 13 is objected to since the syntax could be improved by adding the word "the" between "diagnosing" and "presence."

3. Declaration

A. The Declaration of Mr. Kenji Takamori, filed 4/15/03, was not stated as being submitted under 37 CFR 1.132. However, it is being treated as such. The Declaration was found persuasive, in part, with regard to broadening the scope of the invention to include practicing the claimed method for the examination of diseases other than for those patients undergoing hemodialysis, specifically, atopic dermatitis. Regardless of this Declaration, the Examiner has separately concluded that Applicants deserve the full scope of the diseases presently claimed in the invention. This Declaration is not found persuasive, however, with regard to calculating the ratio of any opioid peptides other than β-endorphin (μ-opioid peptide) and dynorphin A (κ-opioid peptide), or for measuring these ratios in any blood cell, body fluid, or tissue, other than peripheral blood (serum), as discussed below in the rejection under 35 USC 112, first paragraph.

4. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 1, 3, 4 and 6 remain rejected and new claims 12 and 13 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-4 of the Office Action dated 10/21/02. Generally, the rejection states that Applicants are only enabled for a method of examining pruritis in a patient undergoing hemodialysis by measuring β-endorphin (μ-peptide), Leu-enkephalin (δ-peptide) and dynorphin A (κ-peptide) levels in peripheral blood. The Office Action also states that Applicants are not enabled for examining all diseases by measuring all opioid peptides from any blood cell, body fluid or tissue other than peripheral blood.

Applicants argue that when the ratio of either μ – or δ-opioid peptides to κ-opioid peptides in a patient is greater that that found in a healthy patient, the result is pruritis and that this ratio can be tested and adjusted for any of the pruritic conditions that are accompanied by an increase in the calculated ratio. Applicants argue that the claims, as amended, call for diagnosing opioid-based pruritis and not for diagnosing the underlying condition or disease and that the claims have been rewritten to emphasize this fact. Applicants also submit a Declaration by Mr. Kenji Takamori (Paper No. 11). This Declaration states that by following the steps in Example 2 of the instant specification, one of ordinary skill in the art can practice the invention over a variety of pruritic diseases, far beyond hemodialysis, therefore, enabling Applicants' original disclosure.

These arguments have been considered and are persuasive in part. The Examiner does agree with Applicants in that the full scope of the claims regarding examining or diagnosing a disease to determine that it is opioid-based is enabled. As argued by Applicants, the claims do not recite a method of diagnosing the underlying condition or disease, nor how to treat any of these diseases or conditions. The claims simply provide a means to determine if a disease or condition is opioid-based. Therefore, the part of the rejection in the Office Action dated 10/21/02 which limits the claims to hemodialysis (as well as, now, atopic dermatitis as discussed in the Takamori Declaration), has been withdrawn as the Examiner has concluded that this method could be used to diagnose whether or not any disease is opioid-based, regardless of intended treatment.

However, this rejection is maintained with regard to Applicants claiming measuring any and all μ – or δ-opioid peptides, or nociceptin, in any blood cell, body fluid, or tissue. Applicants have not specifically discussed this part of the rejection other than stating that they have found that when the ratio of either μ – or δ-opioid peptides to κ-opioid peptides in a patient is greater that that found in a healthy patient, the result is pruritis. It is clear that μ-opioid (β–endorphin), or δ-opioid (enkephalin) peptides are involved in itching, for example as seen on page 3, lines 10-12 of the specification, and it would be

expected that measuring the concentration of either of these peptides to a κ-opioid peptide would allow one to determine opioid-based pruritis. However, Applicants have not provided any guidance or working examples that determining any κ:κ ratios, including that involving nociceptin, would be indicative of an opioid-based pruritis, nor would this conclusion be predictable in absence of this guidance or working examples.

This rejection is also maintained with respect to Applicants calculating opioid peptide ratios in any component other than peripheral blood. Applicants have not addressed this issue. To summarize this part of the rejection, Applicants have provided no guidance or working examples that determining opioid ratios in blood cells, body fluids, or tissue would be indicative of a pruritis-based disease. It is not known how, for example, measuring peptide concentrations in lymph or aqueous humor (body fluids), in the liver (tissue), or in a platelet (blood cell) would be indicative of pruritis in the hand. Applicants have only demonstrated (Example 2 of the specification) that opioid peptide levels in peripheral blood (i.e. serum) would be indicative of pruritis. Without further guidance, it would not be predictable to the artisan that the ratio of opioid peptides in all blood cells, body fluids or tissue can be used to examine or diagnose opioid-based pruritis.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming measuring any and all κ opioid peptides (κ:κ ratio), including nociceptin, or by measuring opioid ratios in any blood cell, body fluid, or tissue other than peripheral blood. Applicants have not provided any guidance or working examples that determining any κ:κ ratios, including the use of nociceptin, would be indicative of an opioid-based pruritis, nor have Applicants provided any guidance or working examples demonstrating that measuring opioid ratios in blood cells, body fluids, or tissue would be indicative of a pruritis-based disease. In the absence of this guidance and working examples, it would not be predictable to the artisan that a κ:κ peptide ratio, as well as any blood cell, body fluid, or tissue, could be used to determine whether or not a disease is opioid-based. It is believed that all pertinent arguments have been addressed.

5. Claim Rejections - 35 USC § 112, first paragraph – written description

A. The rejection of claims 1-4 and 6 under 35 USC 112, first paragraph, has been withdrawn in view of Applicants' arguments that the claims as written only call for diagnosing opioid-based pruritis and not for diagnosing the underlying condition or disease. The Examiner agrees that sufficient written description of the claimed methods exists.

6. Conclusion

A. No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
June 27, 2003

ROBERT LANDSMAN
PATENT EXAMINER